UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/528,682	03/20/2000	Mariagrazia Pizza	0342.105	5794

27476 7590 12/07/2004

Chiron Corporation
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097

EXAMINER	
BORIN, MICHAEL L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 12/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/528,682	PIZZA ET AL.	
	Examiner	Art Unit	
	Michael Borin	1631	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 November 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet.*

6. ☒ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *7-30.*

   Claim(s) withdrawn from consideration: *31,32.*

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Michael Borin, Ph.D.
Primary Examiner
Art Unit: 1631

In regard to Fig. 12: Examiner maintains that Fig. 12 represents new matter. Nowhere in specification applicant indicated possession of mutants of the particular sequences described in the Domenighini reference. The Domenighini reference itself is used in specification not to direct to particular sequences, but to direct to one particular residue of interest that this suggestion suggests to mutate. The disclosure as filed addresses strains of LT in general (p. 5, lines 5-7) and does not reduce the genus to particular species addressed in Domenighini.

Consequently, amendment to specification suggested by applicant is not entered as it represents new matter as well.

In regard to rejection of claims 7-29 under 35 U.S.C. 112, first paragraph, as addressing 8-meres of SEQ ID No. 1, and thus containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention: Examiner maintains that the claims have not addressed particular species, fragments of particular size of particular SEQID No. 1. All that is described in specification as filed are fragments of LT-A in general. See MPEP 2163.05:

The introduction of claim changes which involve narrowing the claims by introducing elements or limitations which are not supported by the as-filed disclosure is a violation of

the written description requirement of 35 U.S.C. 112, first paragraph. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967) ("If n-propylamine had been used in making the compound instead of n-butylamine, the compound of claim 13 would have resulted. Appellants submit to us, as they did to the board, an imaginary specific example patterned on specific example 6 by which the above butyl compound is made so that we can see what a simple change would have resulted in a specific supporting disclosure being present in the present specification. The trouble is that there is no such disclosure, easy though it is to imagine it.") (emphasis in original).

Note that all Domenighini reference was used for, in the much recited section of specification (p. 5, lines 25+), is to point at location of Ala residue in a particular location. Nowhere does specification as filed demonstrates possession of fragments of particular size of particular sequence, SEQ ID No. 1.

In regard to rejection of claims 7-29 under 35 U.S.C. 112, first paragraph, as addressing polynucleotides encoding any other polypeptides comprising certain fragments of LT-A, Examiner maintains that DNA encoding protein, addressed in "fifth apect" of the invention, reads on DNA encoding full-length protein, but not on DNA encoding any other polypeptides and comprising certain fragments of the protein. In addition,, as addressed above, specification neither demonstrates possession of fragments of particular size of particular sequence, SEQ ID No. 1, nor nucleic acids encoding therefor.

Enablement rejection of claims 7-29 under 35 U.S.C. 112, first as containing subject matter is maintained. Applicant submits that the prior art references submitted to demonstrate toxicity of fragments with replaced Ala-72 are "entirely irrelevant" as long as applicant pointed out which residue (Ala-72) is to be mutated. Examiner disagrees. The instant application demonstrates that full length LT-A has reduced toxicity as compared to wild-type, (Figs 4,5), but does not demonstrate any octamers of LT-A that are detoxified compared to wild type LT-A. Prior art, on the other side, teaches that LT-A derivatives having Ala72 replaced with Arg72 remain to be toxic. Further, there is no description in the claims or specification sufficiently identifying epitope sequence. Consequently, there is no guidance on what fragments are required to maintain immunogenecity and, at the same time, possess reduced toxicity.

In regard to re-introduced art rejections, please note that applicant amended claims to broaden their scope from particular fragments to any 8-meres. Consequently the art rejections of record were re-introduced and it was noted that applicant's amendment necessitated the new grounds of rejection.